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Aliphatic Fluorine Compounds

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Rapid expansion in the field of aliphatic fluorine chemistry during the past decade was further accelerated by war demands for the thermally stable, chemically inert organic compounds of fluorine. The extent of war-inspired research on fluorine chemistry is attested to by the fact that the entire issue of "Industrial and Engineering Chemistry" for March, 1947 was devoted to this subject (1).

Outstanding among these developments are improved fluorine cells, making fluorine readily available for the first time, and a new method of direct fluorination using cobalt trifluoride or silver difluoride. The latter process comprises passing a vaporized hydrocarbon, diluted with nitrogen, over a bed of cobalt trifluoride at 225°-350°C. at which temperature the cobalt trifluoride is converted slowly to cobalt difluoride. The liberated fluorine completely and smoothly replaces all hydrogens and saturates the double bonds of the hydrocarbon molecule. The compound thus formed, containing only carbon and fluorine, is called a fluorocarbon. This new method has made possible the preparation of many higher fluorocarbons, such as perfluoroheptane, C_7F_{16}, which were unknown previously.

$$C_7H_{16} \xrightarrow{CoF_3} C_7F_{16} + HF + CoF_2$$

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Fluorocarbon chemistry has great possibilities, and the use of these compounds as high-temperature lubricants, insulating fluids, and polymer intermediates is being studied.

Commercial Fluorine Compounds

The earliest industrial application of aliphatic fluorine compounds was the development of the Freons as commercial refrigerants in 1930 (2). Freon, CCl_2F_2, and the related chlorofluoromethanes and ethanes are ideal refrigerants, being chemically inert, nontoxic, noncorrosive, and easily compressible gases. They are prepared by the substitution of fluorine for chlorine in the commercially available carbon tetrachloride and related compounds.

$$CCl_4 + HF \xrightarrow{SbF_3} CCl_2F_2 \text{ (Freon 12)}$$

Economical production of the Freons depends upon a cheap, continuous method of making hydrogen fluoride, which is now available. Hydrogen fluoride is used today in large commercial quantities in the refining of petroleum and in the production of hydrocarbons. In contrast to the extreme stability of polyfluoroalkanes, monofluoroalkanes are quite unstable.

A more recent commercial application of aliphatic fluorine compounds was the

development in 1941 of Teflon, a super-resistant tetrafluoroethylene polymer, by E. I. du Pont de Nemours & Co. (1,3). One commercial method of preparing the monomer utilizes the reaction:

$$2CHClF_2 \xrightarrow[\triangle]{} CF_2=CF_2 \xrightarrow[\triangle]{\text{pressure}} \text{polymer.}$$

Extensive investigation of the polymerization of other fluorinated olefins is going on apace.

Pioneering Work of Swarts

These commercial developments and the concurrent scientific investigations of aliphatic fluorine compounds carried on during the past twenty years are greatly indebted to the painstaking and thorough pioneering research of the Belgian chemist, Frederic Swarts (4). From about 1890 until his death in 1940, he and his students contributed scores of papers on the preparation and properties of aliphatic fluorine compounds.

One of Swarts' contributions was the preparation of aliphatic fluorine compounds by the substitution method, using antimony trifluoride, silver fluoride, mercurous fluoride, and other fluorinating agents; others included the preparation of fluorinated alcohols, amines, ethers, esters, acids, anhydrides, acid chlorides, amides, ketones, halides, and olefins. The following equations illustrate some of these reactions and the chemistry involved:

$$CHBr_2CH_2Br \xrightarrow{SbF_3} CHF_2CH_2Br$$

$$CHF_2CH_2I \xrightarrow{HgO} CHF_2CH_2OH$$

$$CHF_2CH_2OH \xrightarrow{O} CHF_2COOH$$

$$m\text{-}NH_2C_6H_4CF_3 \xrightarrow{O} CF_3COOH \xrightarrow{PCl_5}$$

$$CF_3COCl \xrightarrow{NH_4OH} CF_3CONH_2$$

$$CF_3COCH_2COOC_2H_5 \xrightarrow{\text{dil. acid}} CF_3COCH_3 \xrightarrow{H_2}$$

$$CF_3CHOHCH_3 \xrightarrow{PBr_3} CF_3CHBrCH_3$$

$$CHF_2CH_2I \xrightarrow{NH_3}$$

$$CHF_2CH_2NH_2 \text{ and } (CHF_2CH_2)_2NH$$

$$CBrF_2CH_2Br \xrightarrow{-HBr} CF_2=CHBr$$

$$CBrF_2CH_2Br \xrightarrow{Zn} CF_2=CH_2$$

$$CF_3COC_5H_{11} \xrightarrow{CH_3MgI} CF_3(CH_3)_2COH \xrightarrow{PBr_3}$$

$$CF_3(CH_3)_2CBr \xrightarrow{-HBr} CF_3(CH_3)C=CH_2$$

$$CBrF_2CH_2Br \xrightarrow{NaOC_2H_5} C_2H_5OCF_2CH_2Br$$

$$(CF_3CO)_2O \xrightarrow[H_2]{[Pt]} CF_3CH_2OH$$

Swarts also correlated the physical constants of these fluorine compounds, showing the influence of fluorine on the boiling points, densities, and refractive indices. The replacement of each bromine atom by fluorine lowers the b.p. about 70°C.; the replacement of each chlorine atom lowers the b.p. about 40°C.

The extreme negativity of fluorine greatly influences the chemical properties of fluorinated functional organic compounds, such as acids, alcohols, and amines. For example, trifluoroacetic acid is a very strong acid. Trifluoroethyl and difluoroethyl alcohol are quite acidic, while the corresponding amines are very weak bases. Gilman and Jones (5) have prepared trifluoroethyl amine, which is a sufficiently weak base to form a diazo compound.

$$CF_3CN \xrightarrow{H_2} CF_3CH_2NH_2 \xrightarrow{HNO_2} CF_3CHN_2$$

Taking up where Swarts left off, Henne and co-workers, since about 1930, have extended aliphatic fluorine chemistry to the propane and butane series and have developed many new methods and techniques (6). Outstanding contributions have been the preparation and actinic chlorination of the compounds $CF_3CH_2CH_3$ and $CF_3CH_2CH_2CH_3$, the use of mercuric fluoride or a mixture

of mercuric oxide and hydrogen fluoride as a fluorinating agent, a new method of preparing fluorinated acids, the addition and substitution of chloro-olefins by hydrogen fluoride, and the addition of fluorine to chlorinated olefins by reaction with lead tetrafluoride.

$$CCl_2{=}CHCH_2CH_3 \xrightarrow{HF}$$

$$CF_3CH_2CH_2CH_3 + Cl_2 \xrightarrow{light}$$

$CF_3CH_2CH_2CH_2Cl$ and $CF_3CH_2CHClCH_3$

$$CHCl_2CH_2CH_3 \xrightarrow{HgF_2} CHF_2CH_2CH_3$$

$$CCl_3CHClCH_3 \xrightarrow{HgO + HF} CF_3CHClCH_3$$

$$CF_3CCl{=}CCl_2 \xrightarrow{O} CF_3COOH$$

$$CCl_2{=}CHCH_3 \xrightarrow{HF}$$

$$CClF_2CH_2CH_3 \xrightarrow{HF} CF_3CH_2CH_3$$

$$CF_3CCl{=}CCl_2 \xrightarrow{PbF_4} CF_3CClFCCl_2F$$

Henne has described the pressure equipment necessary for fluorination work and the need for copper, nickel, or stainless steel equipment in handling hydrogen fluoride reactions.

Recent Advances

More recently, Henne and his coworkers have prepared several new fluorinated ester condensation products such as ethyl difluoroacetoacetate, trifluoroacetylacetone, and hexafluoroacetylacetone (7). They also prepared the fluorinated ester, ethyl 2,2-difluorobutyrate, which on hydrolysis yielded 2-monofluorocrotonic acid instead of the expected 2,2-difluorobutyric acid. Other new acids prepared were 1,1-difluoropropionic acid, 4,4-difluorohexanoic acid, and perfluoroadipic acid (8).

The addition of hydrogen fluoride to unsaturated bonds has been carried out by Grosse and Linn (9).

$$CH_2{=}CH_2 \xrightarrow{HF} CH_3CH_2F$$

$$CH{\equiv}CH \xrightarrow{HF} CH_2{=}CHF \xrightarrow{HF} CH_3CHF_2$$

Hass, McBee, and co-workers, since about 1940, have extended the work of Henne on the aliphatic fluorine compounds of ethane, propane, and butane, especially in the realm of vapor phase fluorinations with hydrogen fluoride and fluorinations with hydrogen fluoride at higher temperatures and pressures. Very useful methods for the thermal bromination and chlorination of $CF_3CH_2CH_3$ and $CClF_2CH_2CH_3$ have been described. Some of the results of extensive research by these investigators during the war have been published (1, 10).

$$CH_2{=}CCl_2 \xrightarrow{HF} CH_3CF_3$$

$$CHCl{=}CCl_2 \xrightarrow{HF} CF_3CH_2Cl$$

$$CF_3CH_2CH_3 \xrightarrow[450°C]{Br_2}$$

$CF_3CH_2CH_2Br$ and $CF_3CHBrCH_3$

$$CClF_2CH_2CH_3 \xrightarrow[350\text{-}400°C]{Cl_2}$$

$CClF_2CH_2CH_2Cl$ and $CClF_2CHClCH_3$

These authors have also prepared such fluorinated ethers as $ROCF_2CHCl_2$, $ROCF_2CH_2Cl$, and $ROCF{=}CHCl$. Also of considerable interest is a series of polyfluorinated dibasic acids and amines. Dichloroperfluorocyclohexene was oxidized to perfluoroadipic acid, $HOOC(CF_2)_4COOH$, which was converted to the ester, amide, and nitrile. The latter upon reduction yielded $NH_2CH_2(CF_2)_4CH_2NH_2$. Of synthetic interest are the difluoroisopropyl halides, $CHF_2CHClCH_3$ and $CHF_2CHBrCH_3$, which were prepared in poor yields.

Bigelow and his students, since about 1930, have developed methods for modifying the violent reaction of elemental fluorine with organic compounds and isolating the many products (11).

$$CH_3CH_3 + F_2 \xrightarrow[\text{Cu gauze}]{N_2}$$

CF_3CHF_2, CHF_2CHF_2, CHF_2CH_2F, CF_4 and C_2F_6

$$CH_3COCH_3 + F_2 \xrightarrow[\text{Cu gauze}]{N_2} CF_3COCF_3,$$

CH_2FCOCH_3, CF_3COF, $(COF)_2$, COF_2 and CF_4.

During this same period, Simons and co-workers have also studied quite extensively direct fluorination and the chemistry of hydrogen fluoride as a condensing agent (11).

In addition to the commercial uses of aliphatic fluorine compounds as refrigerants, polymer intermediates, and insulating fluids, many other uses are anticipated. A comprehensive study of a large number of aliphatic fluorine compounds showed some of them to be effective as anesthetics (12). Sodium fluoroacetate, $CH_2FCOONa$, is a potent rodenticide. While most organic fluorine compounds are nontoxic, fluorinated cyclopropane derivatives and fluorinated alcohols appear to be quite toxic. Investigation of aliphatic fluorine compounds as insecticides is now actively under way.

References

(1) Fluorine Chemistry Symposium (entire issue), *Ind. Eng. Chem.*, 39, 236-433 (March, 1947).

(2) Midgley and Henne, *Ind. Eng. Chem.*, 22, 542 (1930).

(3) Renfrew and Lewis, *Ind. Eng. Chem.*, 38, 870 (1946).

(4) Delépine, *Compt. rend.*, 212, 1057 (1941); *C.A.* 36, 5681 (1942).

(5) Gilman and Jones, *J.A.C.S.*, 65, 1458, 2037 (1943).

(6) Henne in Gilman's "Organic Chemistry," 2nd Ed., John Wiley and Sons, Inc., Vol. I, Chap. 11, pp. 944-964 (1943).
Henne in Adams' "Organic Reactions," John Wiley and Sons, Inc., Vol. II, pp. 49-93 (1944).

(7) Henne et al., *J.A.C.S.*, 69, 1819 (1947).

(8) Henne and Zimmerscheid, *J.A.C.S.*, 69, 281 (1947).

(9) Grosse and Linn, *J.A.C.S.*, 64, 2289 (1942).

(10) McBee et al., *J.A.C.S.*, 69, 944 (1947).

(11) Bigelow, *Chem. Reviews*, 40, 51 (1947).

(12) Robbins, *J. Pharmacol.*, 86, 197 (1946).

New Eastman Organic Chemicals

5882	Adiponitrile BP 143-146°/6mm	500	g...	$ 7.00 D
	$NC(CH_2)_4CN$...MW 108.14			
5921	2-Chlorothiophene BP 126-127.5°	500	g...	8.00 D
	SCH:CHCH:CCl...MW 118.59			
2295	Durene MP 78-80°	10	g...	3.00 B
	1,2,4,5-$(CH_3)_4C_6H_2$...MW 134.21			
P 5934	2-Ethylhexyl Chloride (Pract.) BP 171-173°	1	kg...	2.50 E
	$CH_3(CH_2)_3CH(C_2H_5)CH_2Cl$...MW 148.67			
4607	α-D-Galacturonic Acid $\cdot H_2O$	100	g...	12.00 C
	$C_6H_{10}O_7 \cdot H_2O$...MW 212.16			
5933	5-Methyl-Δ^4-tetrahydrophthalic Acid MP 155-156°	100	g...	7.00 C
	$CH_3C:CHCH_2CH_2CH(COOH)CHCOOH$...MW 184.19			
5916	2-Nitrothiophene MP 42-44°	10	g...	1.50 A
	$SCH:CHCH:CNO_2$...MW 129.14			
5904	Thiophene-2-carboxylic Acid MP 127-129°	10	g...	1.60 A
	SCH:CHCH:CCOOH...MW 128.15			